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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/781,850 | 02/20/2004 | Stevan P. Tofovic | 007278-04 | 1648 |

36234 7590 07/17/2006

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| EXAMINER |
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HUI, SAN MING R

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| ART UNIT | PAPER NUMBER |
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1617

DATE MAILED: 07/17/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/781,850

Applicant(s)

TOFOVIC ET AL.

Examiner

San-ming Hui

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10 May 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1, 2, 4-6, 8-10, 12-14, 16-18, 20-22, 24-26, 28-30, 32-34 and 36 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 2, 4-6, 8-10, 12-14, 16-18, 20-22, 24-26, 28-30, 32-34 and 36 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

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DETAILED ACTION

Applicant's amendments filed May 10, 2006 have been entered. Claims 3,7,11,15,19,23,27,31, and 35 have been cancelled.

Claims 1-2, 4-6,8-10, 12-14, 16-18, 20-22, 24-26, 28-30, 32-34, 36 are pending.

The outstanding rejection under 35 USC 112, second paragraph is withdrawn in view of the amendments filed May 10, 2006 since the claims have been cancelled.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-2, 4-6,8-10, 12-14, 16-18, 20-22, 24-26, 28-30, 32-34, 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over US2003/0027751('751) and US2001/0056068 ('068).

'751 teaches 2-methoxyestradiol as useful in treating pulmonary hypertension (See paragraph [0175] and [0179]).

'068 teaches the method of treating pulmonary hypertension (a nitric oxide deficiency disorder) using estradiol, estriol and estrone (See claims 1, 7, 14, and 16). '068 also suggests the use of continuous or prolong release dosage form (See paragraph 0119). Examiner notes that estradiol is a prodrug of estradiol metabolite.

The primary references do not expressly teach both 2-methoxyestradiol and estradiol be used together in the method of treating pulmonary hypertension.

It would have been obvious to one of ordinary skill in the art at the time of invention to employ both 2-methoxyestradiol and estradiol be used together in the method of treating pulmonary hypertension.

One of ordinary skill in the art would have been motivated to employ both 2-methoxyestradiol and estradiol be used together in the method of treating pulmonary hypertension. Concomitantly employ both agents, which are known to be useful in treating pulmonary hypertension, in a single method of treating the very same disorders would be *prima facie* obvious (See *In re Kerkhoven* 205 USPQ 1069). Examiner notes that the resulting mechanism of estradiol metabolites recited are considered as intrinsic properties within the metabolites of estradiol.

Response to Arguments

Applicant's arguments filed May 10, 2006 averring '751's failure to teach 2-methoxyestradiol in treating pulmonary hypertension have been fully considered but

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they are not persuasive. Examiner notes that '751 teaches 2-methoxyestradiol can be used in conjunction with anti-angiogenic factors in the treatment of pulmonary hypertension. Since the claims recite the transitional phrase "comprising", the claims are permitted any compounds to be added to the method recited. Therefore, possessing the teachings of the cited prior arts, one of ordinary skill in the art would have been motivated to concomitantly employ the herein claimed agents in the method of treating pulmonary hypertension.

Applicant's arguments filed May 10, 2006 averring the prior arts cited in the previous office action mailed August 5, 2005 have been considered, but are not found persuasive since the rejection have been withdrawn. Furthermore, the arguments are not seen to be relevant to the rejection set forth in the office action.

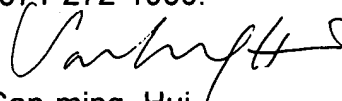
THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to San-ming Hui whose telephone number is (571) 272-0626. The examiner can normally be reached on Mon 9:00 to 1:00, Tu - Fri from 9:00 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, PhD., can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.


San-ming Hui
Primary Examiner
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